BP 36: Cell Adhesion and Migration, Multicellular Systems II

Time: Friday 9:30–12:00 Location: H 1028

Invited Talk BP 36.1 Fri 9:30 H 1028

Physical forces driving migration, division and folding in epithelial sheets — •Xavier Trepat — IBEC, Baldiri Reixac 15-21, 08028 Barcelona

Biological processes such as morphogenesis, tissue regeneration, and cancer invasion are driven by collective migration, division, and folding of epithelial tissues. Each of these functions is tightly regulated by mechanochemical networks and ultimately driven by physical forces. I will present maps of cell-cell and cell-extracellular matrix (ECM) forces during cell migration and division in a variety of epithelial models, from the expanding MDCK cluster to the regenerating zebrafish epicardium. These maps revealed that migration and division in growing tissues are regulated cooperatively. I will also present direct measurements of epithelial traction, tension, and luminal pressure in three-dimensional epithelia of controlled size and shape. By examining epithelial tension over time-scales of hours and for nominal strains reaching 300%, we establish a remarkable degree of tensional homeostasis mediated by cellular adaptations.

BP 36.2 Fri 10:00 H 1028

Simultaneous Modeling of Random Crawling and Internal Polarization of Motile Amoeboid Cells — •Sergio Alonso[1], Maike Stange[2], and Carsten Beta[2] — [1]Department of Physics, Universitat Politecnica de Catalunya, Barcelona, Spain — [2]Institute of Physics and Astronomy, Universität Potsdam, Potsdam, Germany

The amoeboid motion of certain cells gives rise to different dynamics depending on the level of starvation. This motion is correlated with the patterns of diverse biochemicals in the interior of the cells. We compare first the displacement and the velocity of vegetative and starving cells of Dictyostelium discoideum with a simple model of individual cells. Second, the deformations of the membrane is studied in the numerical model and in the living cells, and finally, we study the patterns originated in the interior of the simulated cells and compare them with the actin patterns observed in the experiments. Therefore, we fit and adapt the parameter values of the model to correctly account for the motion of the centre of mass of the cell and the intracellular pattern formation.

BP 36.3 Fri 10:15 H 1028

Intricate features of 3D cancer cell invasion — •Frank Sauer[1], Steffen Grosser[2], Josef A. Käs[2], and Claudia T. Mierke[1] — [1]Biological Physics Division, Peter Debye Institute for Soft Matter Physics, University of Leipzig, Germany — [2]Soft Matter Physics Division, Peter Debye Institute for Soft Matter Physics, University of Leipzig, Germany

The invasion and the motility of cells into 3D tissues is often connected to cell shape changes and pathologists typically diagnose cancer from cell shape or tissue architecture anomalies. However, the correlation between cell shapes and tissue properties and their influence on cancer cell motility is still not well understood. We developed live invasion assays that allow us to analyze the 3D migration pathway of single cells or cells invading from spheroids into tunable collagen gels on statistically relevant cell numbers. Cell shape information can be correlated with migration patterns, invasion depth and matrix properties. Our results show that the invasiveness and the aspect ratio of single invasive MDA-MB-231 cells is drastically reduced by increasing collagen concentration, whereas clusters of the same cells show a distinct contraction and densification of the collagen network prior to invasion followed by a subsequent degradation. On spheroids from non-invasive MCF7 cells only minor network deformations and no invasion or fiber degradation was observed. Our findings support the view that the mechanical properties of the extracellular matrix are a key factor to initiate cancer cell evasion from cell masses such as spheroids, however, they can also act as an obstacle for single cell migration.

BP 36.4 Fri 10:30 H 1028

The Physics of Blastoderm Flow during Early Gastrulation of Tribolium castaneum — •Stefan Münster[1,2,3], Alexander Mietke[1], Akanksha Jain[2], Pavel Tomancak[2], and Stephan Grill[1,3] — [1]MPI for Physics of Complex Systems — [2]MPI of Molecular Cell Biology and Genetics — [3]TU Dresden

The early embryo of the red flour beetle, Tribolium castaneum, initially consists of a single-layered blastoderm covering the yolk uniformly that differentiates into an embryonic rudiment as well as extraembryonic amnion and serosa. The germband anlage forms inside the egg during gastrulation when the embryonic rudiment condenses and folds along the ventral midline; this process is accompanied by large-scale flow and expansion of the extraembryonic serosa which ultimately covers the entire surface of the egg, thus engulfing the growing embryo. The mechanical properties of these tissues and the forces governing these processes in Tribolium, as well as in other species, are poorly understood. Here, we present our findings on the dynamics of myosin in the early blastoderm of Tribolium using multiview lightsheet live imaging of transiently labeled wild type embryos. We quantitatively measure the global distribution of myosin throughout the flow phase and present a physical description that couples the contractile forces generated by myosin to the mechanical properties of the blastoderm. In particular, we describe the overall tissue as a thin, actively contractile, viscous bulk medium that exhibits friction with the vitelline membrane. This description accurately captures the large-scale deformation the tissue undergoes during the initial stages of gastrulation.

BP 36.5 Fri 10:45 H 1028

Force generation during collective migration of bacteria — •Benedikt Sabass — Forschungszentrum Jülich, Germany

Bacterial migration, aggregation, and even host infection depend on the generation of mechanical force. Here, we present a first study of bacterial cell-substrate traction using Myxococcus xanthus as a model organism. M. xanthus exhibits two common mechanisms of motility, namely, twitching and gliding. We find that these two mechanisms lead to complementary dynamics and traction patterns. Twitching leads to local, uncoordinated traction while gliding in groups allows for collective emergence of directional traction. The forces generated by each cell are significantly upregulated when cells contact each other in groups, which highlights the importance of cell-cell signaling for collective motility.

Force generation by groups of migrating bacteria
B. Sabass, M.D. Koch, G. Liu, H.A. Stone, J.W. Shaevitz
PNAS, 114(28) : 7266, 2017

BP 36.6 Fri 11:00 H 1028

Integrated Heart-on-a-Chip systems: *In situ* characterization of contractile forces in 3D cardiac μ-tissues — •Oliver Schneider, Stefanie Fuchs, Christopher Probst, and Peter Loskill — Department of Cell and Tissue Engineering, Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, Stuttgart, Germany

Human induced pluripotent stem (iPS) cells possess the power to revolutionize medicine and basic biological research by opening pathways for individualized medicine and large-scale animal-free drug testing. Over the last years, microfluidic Organ-on-a-Chip (OoC) systems evolved from a conceptual idea to a feasible alternative for animal models. OoCs combine iPS-based tissues with microfabrication technologies to create microphysiological *in vitro* models featuring human genetic background, physiologically relevant tissue structure and "vasculature-like" perfusion. Most of these systems, however, lack the ability to thoroughly analyze the integrated tissues and their response to administered drugs. We present a novel integrated device enabling the parallelized cultivation and characterization of human cardiac microtissues in a physiological, precisely controlled environment. By combining traction force microscopy with microfluidic OoC-systems, we are able to extract *in situ* information about the spatial and temporal force distribution in cardiac microtissues. The developed system enables the multiplexed automated analysis of many individualized tissues in parallel, thus bridging the gap from basic tissue creation to viable big data collection.

BP 36.7 Fri 11:15 H 1028

Dynamics of Cell Jamming: Disentangling the Shape and Density Dependences — •Jürgen Lippoldt, Steffen Grosser, Paul Heine, Linda Oswald, and Josef Käs — Peter Debye Institute for Soft Matter Physics, University Leipzig, Leipzig, Germany

Cellular dynamics have been shown to display characteristics of jamming transitions, which originally had been observed as a function of

cell number density (Angelini et al., PNAS 2011). Recently, the Self-Propelled Voronoi (SPV) model has predicted a density-independent transition as a result of the counter play of adhesion and contractile forces (Bi et al., Nat. Phys. 2015), visible in the dimensionless shape parameter.

We use cell tracking combined with Voronoi tessellation of the nuclei to estimate the probability of T1 transitions and neighborhood exchanges. Thereby, we can describe the local fluidity of a cell layer and look for the onset of cellular jamming. A moderately high density is required for epithelial-like MCF-10A cells to jam. Within this high-density regime, the correlation of fluidity and shape of the individual local cells is stronger than the correlation of fluidity and local density. Mesenchymal-like MDA-MB-231 cells stay fluid even for very high densities and never reach the round configurations that correlate to jamming for epithelial-like MCF-10A. In co-culture, both cell types demix and MDA-MB-231 cells form unjammed islands within the jammed collective of MCF-10A cells.

BP 36.8 Fri 11:30 H 1028

Temperature gradients characterize, counteract and rescue P granule segregation in *C. elegans* — •Anatol W. Fritsch[1], Matthäus Mittasch[1], Carsten Hoege[1], Frank Jülicher[2], Anthony Hyman[1], and Moritz Kreysing[1] — [1]MPI-CBG, Dresden, Germany — [2]MPI-PKS, Dresden, Germany

Recent studies report on membrane-less condensates in cells, that are formed by liquid-liquid phase separation. In *C. elegans* zygotes condensates, named P granules, segregate asymmetrically to one daughter cell during the first cell division. This process is involved in the development of a functional germ line. More specifically, the asymmetric localization of P granules depends on a protein gradient of MEX-5 along the long axis of the zygote. MEX-5 in turn, is thought to act through an mRNA competition mechanism and locally regulates the phase separation of the of the condensates.

Using a strategy based on the physical principles of phase-separation, we are able to rescue the asymmetric localization of P granules in MEX-5 RNAi mutants with defective segregation *in vivo*. We replace the protein gradient with a localized temperature gradient that mimics the physical mechanisms of the local regulation in phase separation. Furthermore, with this approach, we are able to invert the endogenous spatial distribution of P granules in zygotes. This enables us to study the dynamics of *in vivo* phase separation via controlled physical perturbations. In this study we conclude, that P granule segregation is a spatially tuned, diffusive-flux dependent, evaporation-condensation phenomenon.

BP 36.9 Fri 11:45 H 1028

Inversion of rod photoreceptor nuclei improves retinal light transmission by 50% — •Kaushikaram Subramanian[1], Martin Weigert[1], Heike Petzold[1], Marius Ader[2], Irina Solovei[3], and Moritz Kreysing[1] — [1]MPI-CBG, Dresden, Germany — [2]CRTD, Dresden, Germany — [3]LMU, Munich, Germany

Vertebrate retina has a puzzling inverted structure, with 100s of microns of living neural tissue in the light path before its detection by rods and cones. Large number of rods result in densely packed, light scattering nuclei. In nocturnal mammals rods postnatally undergo a hallmark process of nuclear architecture inversion [1]. Previous studies suggest,reduced forward light scattering in isolated rod nuclei and their predicted light focusing was experimentally verified [2].

Now, with high-throughput analysis of wild type and transgenic mouse retina nuclei we establish causality in large angle light scattering and sub nuclear architecture. Using modulation transfer analysis at tissue level, we demonstrate nearly 50% reduction in image detail transfer (Strehl ratio) in transgenic retina lacking nuclear inversion. Modelling and simulation of light propagation reveal a mechanistic relation between single cell scattering and emergent tissue optics. Finally, behavioral studies confirm the visual benefit of inverted nuclear organization for motion detection in low light conditions. Thus, inverted nuclear architecture in mouse retina conclusively improves retinal image transfer and visual function.

References: [1] Solovei et al, Cell(2009) [2] Błaszczak et al, Opt Express(2014) [3] Solovei, et al, Cell(2013)